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Attorney Docket No. 387978007WO0

International Appn No. **PCT/US04/20338**
International Filing Date: **24 June 2004**
Priority Date: **25 June 2003**
Title: **Compositions and Methods for Skin Conditioning**
Applicant: **Geron Corporation *et al.***

July 12, 2005

Mail Stop PCT, Attn: IPEA/US
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sirs:

In response to the Written Opinion mailed April 12, 2005 in the above-referenced application, the applicants submit the following amendments and comments.

I. Amendments

Enclosed are amended claim pages 47-50, to replace original claim pages 47-51 in the application, and marked pages showing the amendments.

Independent claim 1 has been amended to recite that the formulation includes an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant (as provided in original claim 28 and in the definition of "cosmetic vehicle" in the specification at page 7, lines 28-32) and an ingredient selected from the group consisting of a preservative, an antioxidant, and an antimicrobial agent (as disclosed in the specification at page 15, lines 12-16).

Claims 2-16 are unchanged.

Claims 17-24 are cancelled, and the remaining claims are renumbered accordingly. Claims 25-32 (renumbered as 17-24) are amended to remove the reference to claim 17.

II. The Examination Report

All pending claims were found to have industrial applicability. Claims 11-16 were found to be novel and inventive over the prior art.

The Examiner contended that claims 17-32 lack novelty over U.S. Patent No. 5,663,160. This rejection is rendered moot in view of the cancellation of claims 17-24 and the removal of the reference to independent claim 17 in claims 25-32.

The Examiner further contended that claims 1-10, 28, and 31-32 lack novelty over U.S. Patent No. 6,162,459 (Hu).

Hu discloses a "multitude of compounds" (as characterized by the Examiner) as "enhancers for drug absorption through the skin" (column 3, lines 45-48). There are in fact about 450 such compounds listed at columns 11-16 of the patent.

Independent claim 1 has been amended to recite that the claimed formulation further includes an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant, and an ingredient selected from the group consisting of a preservative, an antioxidant, and an antimicrobial agent. None of these components are disclosed in the Hu patent. (Applicants also note that original dependent claims 29-30, which originally recited such components, were not found to lack novelty over this reference.)

Applicants further note that the "multitude of compounds" disclosed in Hu as "enhancers for drug absorption through the skin" (column 3, lines 45-48) are described as "largely inert by themselves" (column 3, lines 31-33). Therefore, applicants submit that the claims are inventive as well as novel over this reference, which provides no suggestion to select any particular compound(s) from this list of hundreds of "largely inert" compounds for use in a method of skin conditioning.

The Examiner further contended that claims 1-10, 28, and 31-32 lack novelty over PCT Pubn. No. WO 2005/00245. Applicants note that this reference is available as prior art for the purpose of novelty only.

As noted above, independent claim 1 has been amended to recite that the formulation further includes an ingredient selected from the group consisting of a preservative, an antioxidant, and an antimicrobial agent. None of these components is disclosed in the PCT publication.

The Examiner further contended that claims 1-9, 28, and 31-32 lack novelty over Yasukawa *et*

al., *Oncology* **48**:72-76 (1991). This publication describes the application of various compounds to the skin of a test animal (mouse) in a vehicle selected from chloroform and 50% methanol (page 73, first column).

As noted above, independent claim 1 has been amended to recite that the claimed formulation further includes an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant, and an ingredient selected from the group consisting of a preservative, an antioxidant, and an antimicrobial agent*. None of these components are disclosed in the Yasukawa publication.

Moreover, applicants note that the compounds recited in dependent claims 8-9 are not disclosed in the Yasukawa reference, which discloses only astragaloside I.

III. Conclusions

In view of the foregoing, the applicants submit that the now pending claims comply with the requirements of PCT Articles 33(2)-(3).

Respectfully submitted,

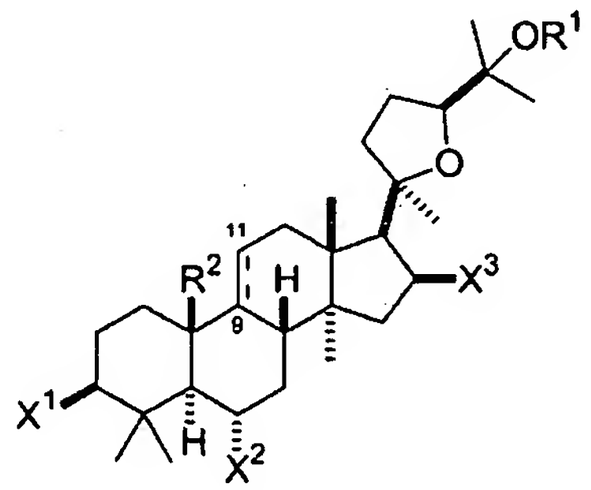
Date: July 12, 2005

LeeAnn Gorthey
Registration No. 37,337

CORRESPONDENCE ADDRESS:
LeeAnn Gorthey
Perkins Coie LLP
P.O. Box 2168
Menlo Park, CA 94026

CLAIMS

1. A method for conditioning the skin, comprising: applying topically to the skin a formulation comprising a compound of formula I:



I

where:

each of X^1, X^2, and X^3 is independently selected from hydroxy, lower alkoxy, lower acyloxy, keto, and a glycoside;

OR^1 is selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside;

wherein any of the hydroxyl groups on said glycoside may be substituted with a further glycoside, lower alkyl, or lower acyl, such that the compound includes a maximum of three glycosides; and

R^2 is methyl and ---- represents a double bond between carbons 9 and 11; or, R^2 forms, together with carbon 9, a fused cyclopropyl ring, and ---- represents a single bond between carbons 9 and 11;

and wherein said formulation further comprises an ingredient selected from the group consisting of an emulsifier, a surfactant, a thickener, a skin emollient, and a lubricant, and an ingredient selected from the group consisting of a preservative, an antioxidant, and an antimicrobial agent.

2. The method of claim 1, wherein said compound includes zero, one, or two glycosides, none of which is substituted with a further glycoside.

3. The method of claim 2, wherein said compound includes zero or two glycosides, none of which is substituted with a further glycoside.

4. The method of claim 1, wherein each said glycoside, when present, is of the D configuration.

5. The method of claim 1, wherein R^2 forms, together with carbon 9, a fused cyclopropyl ring; and ---- represents a single bond between carbons 9 and 11.

6. The method of claim 2, wherein each of X^1 and X^2 is independently selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside, and X^3 is selected from hydroxy, lower alkoxy, lower acyloxy, keto, and a glycoside.

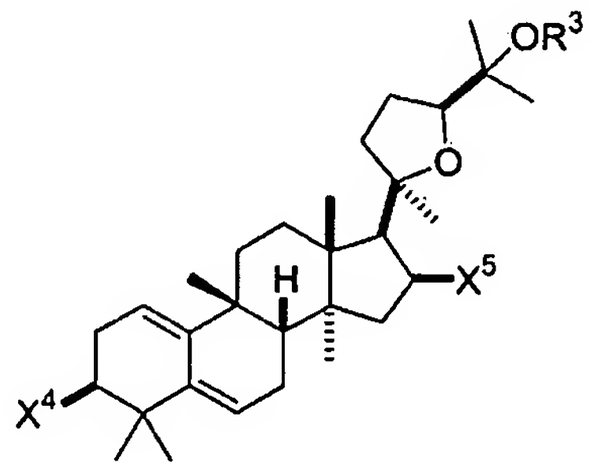
7. The method of claim 2, wherein X^1 is OH or a glycoside, each of X^2 and OR^1 is independently OH or a glycoside, and X^3 is OH or keto.

8. The method of claim 2, wherein the compound is selected from astragaloside IV, cycloastragenol, astragenol, astragaloside IV 16-one, cycloastragenol 6-β-D-glucopyranoside, and cycloastragenol 3-β-D-xylopyranoside.

9. The method of claim 8, wherein the compound is selected from astragaloside IV, cycloastragenol, astragenol, and astragaloside IV 16-one.

10. The method of claim 9, wherein said compound is astragaloside IV.

11. A method for conditioning the skin, comprising: applying topically to the skin a formulation comprising a compound of formula **II**:



II

where:

each of X^4 and X^5 is independently selected from hydroxy, lower alkoxy, lower acyloxy, keto, and a glycoside, and

OR^3 is selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside,

wherein any of the hydroxyl groups on said glycoside may be substituted with a further glycoside, lower alkyl, or lower acyl, such that the compound includes a maximum of three glycosides.

12. The method of claim 11, wherein said compound includes zero, one, or two glycosides, none of which is substituted with a further glycoside.

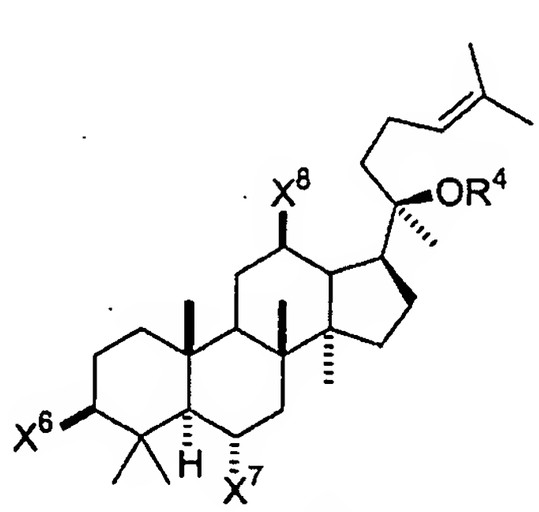
13. The method of claim 11, wherein each said glycoside, when present, is of the D configuration.

14. The method of claim 12, wherein each of X^4 and OR^3 is selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside, and X^5 is selected from hydroxy, lower alkoxy, lower acyloxy, and keto (=O).

15. The method of claim 12, wherein X^4 is OH or a glycoside, and each of X^5 and OR^3 is OH.

16. The method of claim 15, wherein X^4 is OH.

~~17. A method for conditioning the skin, comprising: applying topically to the skin a formulation comprising a compound of formula III:~~



~~III~~

~~where:~~

~~each of X^6, X^7, and X^8 is independently selected from hydroxy, lower alkoxy, lower~~

~~acyloxy, keto, and a glycoside, and~~

~~OR^4 is selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside,~~

~~wherein any of the hydroxyl groups on said glycoside may be substituted with a further glycoside, lower alkyl, or lower acyl, such that the compound includes a maximum of three glycosides.~~

~~18. The method of claim 17, wherein said compound includes zero, one, or two glycosides, none of which is substituted with a further glycoside.~~

~~19. The method of claim 17, wherein each said glycoside, when present, is of the D configuration.~~

~~20. The method of claim 17, wherein each of X^6, X^7, X^8 and OR^4 is independently selected from hydroxy, lower alkoxy, lower acyloxy, and a glycoside.~~

~~21. The method of claim 20, wherein each of X^6, X^7, X^8 and OR^4 is independently selected from hydroxy and a glycoside.~~

~~22. The method of claim 21, wherein each of X^8 and OR^4 is OH, and each of X^6 and X^7 is independently selected from hydroxyl and a glycoside.~~

~~23. The method of claim 22, wherein each of OR^4, X^6 and X^8 is OH, and X^7 is a glycoside.~~

~~24. The method of claim 23, wherein the compound is ginsenoside RH1.~~

17 ~~25~~. The method of claim 1 or 11 ~~any of claims 1, 11, and 17~~, wherein the concentration of said compound in said formulation is from 0.01 to 5% (w/v).

18 ~~26~~. The method of claim 17 ~~25~~, wherein said concentration is from 0.01 to 1% (w/v).

19 ~~27~~. The method of claim 1 or 11 ~~any of claims 1, 11, and 17~~, wherein the

concentration of said compound in said formulation is greater than 0.005% and less than 0.1% (w/v).

20 ~~28~~. The method of claim 1 or 11 ~~any of claims 1, 11, and 17~~, wherein the formulation further comprises one or more additional ingredients selected from the group consisting of an emulsifier, a thickener, and a skin emollient.

21 ~~29~~. The method of claim 20 ~~28~~, wherein the formulation comprises one or more ingredients selected from an emulsifier and a skin emollient.

22 ~~30~~.. The method of claim 21 ~~29~~, wherein the formulation comprises a skin emollient.

23 ~~31~~. The method of claim 1 or 11 ~~any of claims 1, 11, and 17~~, wherein the biological activity of said compound is such that a composition containing the compound at a concentration of 1 µg/ml or less is effective to produce a telomerase activity at least 25% greater than observed in a vehicle control, as measured in a TRAP assay of keratinocyte or fibroblast cells.

24 ~~32~~. The method of claim 1 or 11 ~~any of claims 1, 11, and 17~~, wherein the biological activity of said compound is such that a composition containing the compound at a concentration of 1 µg/ml or less is effective to produce an amount of cell reconfluence in a scratch assay of keratinocytes which is at least 25% greater than that seen in untreated or other control cells.